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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,224	07/28/2003	Cheng J. Cao	DAM 581-02	3741

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US ARMY SOLDIER AND BIOLOGICAL CHEMICAL COMMAND
OFFICE OF THE CHIEF COUNSEL/IP TEAM (BLDG E4435)
5183 BLACKHAWK ROAD
APG, MD 21010-5424

EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,224	CAO ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 14-18* is/are pending in the application.

4a) Of the above claim(s) *1-9,14,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendments filed 10/20/2006 is acknowledged. Claims 10-13 and 19-22 have been canceled.

Drawings

2. The drawings filed 7/28/2003 have been accepted by the examiner.

Specification

3. The disclosure is objected to because of the following informalities: There is a reference number on the left hand side on all pages of the specification, which needs to be removed. Appropriate corrections are required.

Information Disclosure Statement

4. The information disclosure statement filed 7/28/2003 has been considered. An initialed copy is enclosed.

Election/Restrictions

5. Applicants' election without traverse of October 20, 2006 is acknowledged. Applicants elected group I, claims 1-9 and 14-18 without traverse. Applicants further elected the species of the method of claim 15. Claim 16 is dependent from claim 15 and readable thereon. Claims 15-16 are under consideration, claims 1-9, 14 and 17-18 are withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to non elected inventions.

Claim Objections

6. Claims 15-16 are objected to because of the following informalities:

SEQ ID NOS 1-6 has been put in the brackets "[]". Please delete the brackets.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 15-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites " contacting a nucleic acid sequence forming at least a portion of nucleic acid encoding *staphylococcal* enterotoxin A" It is not clear what applicants intends from said recitation. Is the target nucleic acid is a portion of *staphylococcal* enterotoxin A, or one contacts a target nucleic acid with a nucleic acid encoding *staphylococcal* enterotoxin A?

The term "sufficient " in claim 15 is a relative term, which renders the claim indefinite. The term "sufficient" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what amount of thermal cycling is sufficient to amplify the target nucleic acid sequence.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Note: Before stating the rejection below the examiner clarifies the term Real – Time fluorescence PCR:

O'Connell et al. (23rd Army Science Conference, December 2002) define that " Real-time fluorescent PCR works similarly, with. the addition of a third small fragment of DNA to the reaction mixture. The DNA/RNA detection reaction combines standard PCR with a third reagent, a probe DNA molecule that hybridizes to a target sequence between the sequences bound by the two PCR primers. The probe is labeled at one end with a fluorescent dye molecule and at the other end with a molecule that quenches the fluorescence of the dye molecule, such that the proximity of these two molecules results in a quenching of the dye's fluorescence. When a thermostable DNA polymerase extends one of the two primers into the area where the probe is bound, the 5' nuclease activity of Taq DNA polymerase degrades the probe and releases the fluorescent and quencher molecules bound to the probe ends. The separation of the dye and the quencher results in an increase in the overall fluorescence of the sample mixture. A detector in the PCR instrument continually monitors and records the fluorescence present in the sample. Significant accumulation of fluorescence in the sample above background level indicates a positive detection of the target DNA.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Letertre et al. (Molecular and Cellular Probes, vol.17, pp. 139-147, 2003) in light of O'Connell et al. (23rd Army Science Conference, December 2002), and further in view of Borst et al. (Infection and Immunity vol. 61, no. 12, pp. 5421-5425, 1993 and sequence alignment # STAENAB).

Claim 15 is drawn to a method of determining the presence of staphylococcal enterotoxin A gene in a sample, comprising:

contacting a target nucleic acid sequence forming at least a portion of a nucleic acid encoding staphylococcal enterotoxin A, with polymerase chain reaction reagents specific for the target nucleic acid sequence, the polymerase chain reaction reagents including a primer selected from the group consisting of a forward primer having a specific sequence selected from the group consisting of [SEQ ID NO:3], [SEQ ID NO: 4] and combinations thereof and a reverse primer having a specific sequence selected from the group consisting of [SEQ ID NO: 5], [SEQ ID NO: 6] and combinations thereof, a polymerase enzyme, and a nucleic acid probe, wherein the nucleic acid probe further comprises:

a nucleic acid sequence that hybridizes to a portion of the target nucleic acid sequence wherein the portion is unique to the nucleic acid encoding staphylococcal enterotoxin A;

a reporter attached to a 5' end of the nucleic acid probe, said reporter capable of omitting a detectable signal;

a quencher attached to a 3' end of the nucleic acid probe capable of substantially quenching the reporter and prevent omission of the detectable signal, when the nucleic acid probe is intact, wherein the reporter becomes substantially unquenched when the nucleic acid probe is cleaved by the polymerase enzyme during amplification of the target nucleic acid sequence;

amplifying the target nucleic acid sequence by thermal cycling, wherein the thermal cycling is sufficient to amplify the target nucleic acid sequence; and

measuring the level of fluorescence in the sample subsequent to thermal cycling, and further wherein the level of detectable signal is correlated to an amount of the nucleic acid encoding *staphylococcal* enterotoxin A in the sample, thereby quantitatively detecting the nucleic acid encoding *staphylococcal* enterotoxin A in the sample.

Letertre et al. teach a method of determining the presence of *staphylococcal* enterotoxin A gene in a sample using Real-Time Fluorogenic Polymerase Chain

Reaction (PCR), see title and abstract. Letertre et al. teach the step of contacting a target nucleic acid sequence forming at least a portion of a nucleic acid encoding *staphylococcal* enterotoxin A, with polymerase chain reaction reagents specific for the target nucleic acid sequence, the polymerase chain reaction reagents including forward and reverse primers (see page 140, selection of primers and tables 1-3). Letertre et al. teach a nucleic acid sequence that hybridizes to a portion of the target nucleic acid sequence wherein the portion is unique to the nucleic acid encoding staphylococcal enterotoxin A (see page 140, selection of primers and tables 1-3). Letertre et al. teach a set of universal primers, FastStart Taq DNA polymerase, lighter cycle system from Roche Diagnostics and FastStart DNA Master SYBER Green in a Real –Time fluorescence PCR which covers the limitations (such a reporter attached to a 5' end of the nucleic acid probe, said reporter capable of omitting a detectable signal; and a quencher attached to a 3' end of the nucleic acid probe capable of substantially quenching the reporter and prevent omission of the detectable signal, when the nucleic acid probe is intact, wherein the reporter becomes substantially unquenched when the nucleic acid probe is cleaved by the polymerase enzyme during amplification of the target nucleic acid sequence), see page 143. Letertre et al. teach amplifying the target nucleic acid sequence by thermal cycling, wherein the thermal cycling is sufficient to amplify the target nucleic acid sequence (see page 142). Letertre et al. also teach measuring the level of fluorescence in the sample subsequent to thermal cycling, and further wherein the level of detectable signal is correlated to an amount of the nucleic acid encoding staphylococcal enterotoxin A in the sample, thereby quantitatively detecting the nucleic acid encoding staphylococcal enterotoxin A in the sample (see page 143). Letertre et al. do not specifically teach sequences such as SEQ ID Nos: 3, 4, 5 or 6. These deficiencies have been overcome by the teach of Borst et al. (Infection and Immunity vol. 61, no. 12, pp. 5421-5425, 1993 and sequence alignment # STAENAB).

Borst et al. teach primers consisting of sequences from *Staphylococcus aureus* enterotoxin A gene 100% identical to SEQ ID NO: 3 and SEQ ID NO: 5. (see page 5423 and sequence alignment # STAENAB for SEQ ID NO: 3 and NO: 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the teaching of Letertre et al. and Borst et al. to obtain the claimed invention because Letertre et al. teach a method of determining the presence of *staphylococcal* enterotoxin A gene in a sample using a Real –Time fluorescence PCR One of ordinary skill in the art would have been motivated to use the sequences taught by Borst et al. as forward and reverse primers because these primers are the nucleic acids from a portion of nucleic acid encoding *staphylococcal* enterotoxin A . One would have been motivated to use the already known method and primers of the prior art to detect the presence of staphylococcal toxin in a sample.

Status of the Claims

12. No claims are allowed.

Conclusion

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is 571-272-0863. The examiner can normally be reached on Monday-Friday 7:30 AM-5:00 PM If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Jeffery Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Khatol Shahnan-Shah . B.S., Pharm, M.S.
Biotechnology Patent Examiner
Art Unit 1645
December 31, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER